Schizophrenia Bulletin vol. 47 no. 4 pp. 997–1006, 2021
doi:10.1093/schbul/sbab022
Advance Access publication 27 March 2021

A Meta-analysis of Cognitive Remediation for Schizophrenia: Efficacy and the Role of Participant and Treatment Factors

Julia A. Lejeune[1,2], Andrew Northrop[1], and Matthew M. Kurtz*[,1]

[1]Department of Psychology and Program in Neuroscience and Behavior, Wesleyan University, Middletown, CT, USA; [2]Department of Psychiatry, Boston Medical Center, Boston, MA, USA

*To whom correspondence should be addressed; Department of Psychology and Program in Neuroscience and Behavior, Wesleyan University, Middletown, CT 06459, US; tel: 860-685-2072, fax: 860-685-2761, e-mail: mkurtz@wesleyan.edu

The number of randomized, controlled studies of cognitive remediation (CR) for schizophrenia, a therapeutic approach designed to improve cognitive skills and function, has grown substantially over the past 20 years. Active elements of CR treatment, however, remain unknown. The current meta-analysis investigated treatment, study, and participant factors in the size of observed treatment effects. Electronic databases were searched up to May 2020 using variants of the key words "cognitive remediation," "clinical trials," and "schizophrenia." This search produced 73 unique, randomized, controlled trials. Data were independently extracted by 3 reviewers with excellent reliability. Random-effects models were used to assess primary cognitive and secondary symptom and functional outcomes. Moderator analyses investigated the role of a variety of treatment, study, and participant factors. The meta-analysis (4594 participants) revealed that CR produced significant small-to-moderate size improvements in all domains of cognition studied (Hedge's *g*s = .19–.33). and a significant small improvement in function (Hedge's *g* = .21). CR programs that included a discussion ("bridging") group to help apply acquired cognitive skills to everyday life produced larger effects on global cognition and verbal memory. CR programs with strategy-coaching produced larger effects on episodic memory. Sample age, gender, positive, negative, and overall symptoms, and medication dose did not serve as barriers to treatment gains. CR produces small-to-moderate improvements in cognition and function in schizophrenia. Programs of CR that utilize bridging groups and strategy-coaching are more cognitively potent. Future research should focus on ways to modify CR to bolster generalization of cognitive improvements to function.

Key words: cognitive rehabilitation/cognitive training/severe mental illness/psychosis

Introduction

Broad-spectrum cognitive impairments are a core feature of schizophrenia, present at the first episode of psychosis, and remain stable, or worsen, over time.[1–4] Multiple cross-sectional and longitudinal studies have illustrated a small-to-moderate association between cognition and community functioning, including successful social relationships and work,[3–6] and a small but growing number of studies have linked changes in cognition to changes in function over time.[7,8]

Cognitive remediation (CR) is a behavioral intervention consisting of extensive task practice and/or the acquisition of cognitive strategies with the aim of producing sustained changes in cognitive skills that generalize to functioning.[9] Over the past 20 years, there has been marked growth in the number of trials investigating the efficacy of CR in schizophrenia-spectrum disorders with evidence of small-to-moderate CR-related cognitive and functional improvement. However, the diversity of treatment approaches used across studies has made it difficult for opinion leaders to recommend specific approaches to CR as evidence-based practice.[10,11]

CR is often administered as a component of or in addition to broader programs of psychosocial rehabilitation. This adjunctive treatment may impact outcomes of CR, and play an essential role in the transference of cognitive gains to everyday functioning. While previous studies have suggested that this psychosocial context may be essential for optimizing CR and seeing gains in functional outcomes,[12] some have suggested that the nonspecific elements of these contexts, such as social contact or therapeutic engagement, may be responsible for gains in cognition and functioning.[13]

Interventions differ widely with respect to curricula, which may focus on computerized drill-and-practice or

paper-pencil drill-and-strategy training, and the provision of motivational support and/or cognitive strategy coaching while CR exercises are practiced.[13] Many trials have opted to include a "bridging" discussion group separate from the CR training itself, to promote the generalization of cognitive gains to everyday living.[14–16] It remains unknown which, if any, of these treatment features are crucial for CR success.

Two recent meta-analyses have investigated computer-assisted CR approaches. One found a small-to-moderate effect of CR on attention, working memory, positive symptoms, and depressive symptoms, but found no effect of CR on functional outcomes.[17] The second found that intervention modalities delivered with SHG were significantly more effective in improving verbal memory, working memory, and "real-world" cognitive skills than computerized CR alone.[18] However, CR with SHG had no differential impact on clinical symptoms or functional outcomes.[18]

As the largest meta-analysis of CR for schizophrenia to date, including both computerized and non-computerized modalities, the present study was designed to assess the efficacy of CR broadly, and to analyze how multiple factors moderate treatment outcomes. Our primary hypothesis was that CR will produce improvements on measures of cognition (primary outcome). We also predicted that there would be a positive effect of CR on secondary outcomes, such as functioning (both performance-based measures of functional capacity and clinician assessments of community-function), symptoms, and client-experience measures of recovery. With respect to moderators, we hypothesized that the effects of CR would be smaller when delivered as a stand-alone treatment compared to when CR is offered as an adjunct to another form of psychosocial rehabilitation, and that strategy coaching and bridging groups would enhance CR effects.

Methods

Literature Search

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement.[19] Searches were conducted in December 2018 and in May 2020, using the databases PsycINFO and PubMed. See supplementary materials for search strings and figure 1 for a PRISMA flow diagram of search results.

Inclusion and Exclusion Criteria

Articles were included if: (1) RCTs compared a CR intervention with a non-CR control group, (2) published between 1980 (year of publication of DSM-III)[20] and May 2020, (3) published in English, (4) the intervention targeted cognition, with CR accounting for at least 50% of the treatment time, (5) outcomes included a standardized performance-based measure of cognition, (6) at least 70% percent of study participants had a diagnosis of schizophrenia or schizoaffective disorder, and (7) reported post-treatment outcome data as either raw means or least-squares means. Articles were excluded if the CR intervention: (1) included an element of social cognitive or social skills training, or (2) trained on a single cognitive measure. We excluded studies that included a social cognitive training component to their program of CR to better understand the mechanisms of action of treatments targeted specifically at elementary cognitive deficits and their relationship to other key treatment outcomes.

Data Extraction

Data from each included study was independently extracted by pairs amongst the 3 authors (J.A.L., A.N., M.M.K.) using a standardized data extraction spreadsheet. Data extracted included: location/year of the study; premorbid, clinical, and demographic characteristics of the sample; characteristics of the CR intervention and control condition; and outcome measures. Interrater reliability measures of data extracted from a subset of these studies was 98%. Discrepancies between raters were resolved by consensus. If an included study reported more than one comparator group (ie, TAU vs active control), we extracted data from the active control group except when the control treatment was a social cognitive intervention where overlap between CR and the alternative treatment might be significant and obscure the true effects of CR interventions. For studies that accompanied CR with a form of human guidance, a separate distinction was made for human guidance that included strategy coaching. Certain studies complemented a CR intervention with an adjunctive psychosocial rehabilitation program. These adjunctive rehabilitation programs were categorized as either evidence-based or non-evidence-based. Programs (such as cognitive-behavioral therapy and supported employment) were defined as evidence-based in accordance with the Schizophrenia Patient Outcomes Research Team (PORT) psychosocial treatment recommendations.[10]

Outcomes

Cognitive variables were categorized based on the domain they were presumed to assess. Objective cognition measures were organized into 7 domains corresponding to those of the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB)[21]: attention, reasoning and problem-solving, working memory, processing speed, verbal learning and memory, visual learning and memory, and social cognition. Cognitive tests not used in the MCCB but studied in previous

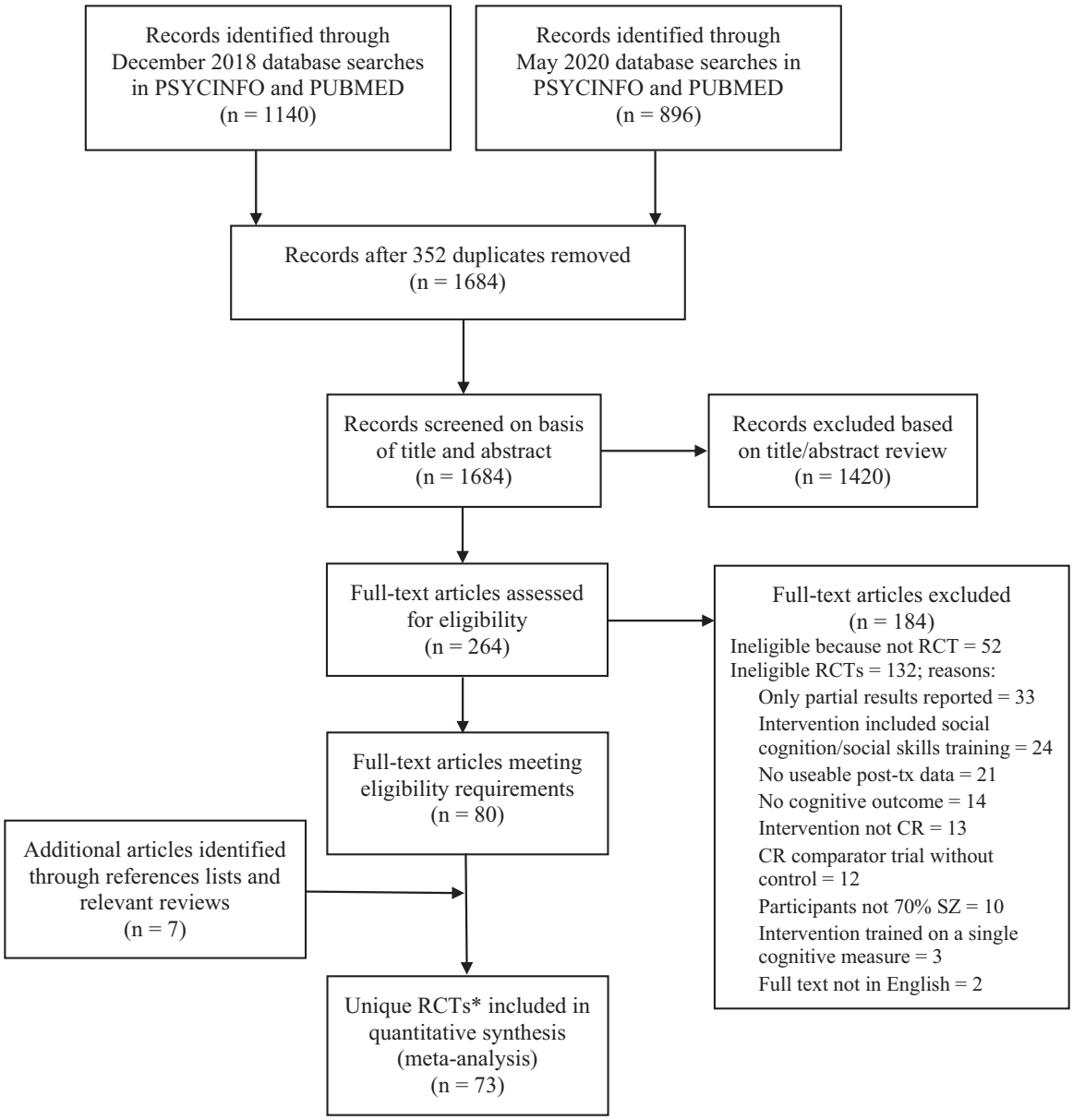

Fig. 1. PRISMA flow diagram. *Multiple published articles representing results from a single RCT were grouped together.

meta-analyses were grouped into these general MCCB domains according to previous practice.[12,17,22] Tests not studied in previous meta-analyses were grouped according to the domain they were presumed to measure. A global cognition domain was formed from MCCB composite scores and from author-derived cognitive summary scores when a majority of the component tests aligned with our test-domain categorizations. For function, performance-based measures of social skill and activities-of-daily living were distinguished from clinician-rated and/or self-reported psychosocial outcome scales.[23] Lastly, we also included measures of clinical symptoms and recovery (eg, self-esteem, self-efficacy).

Statistical Analysis

Effect-Size Calculation. Effect-size analyses were conducted according to procedures suggested by Rosenthal[24] and Hedges and Olkin,[25] using Comprehensive Meta-Analysis v. 2 software.[26] For purposes of the present study, the Hedge's *g* score was defined as the difference between intervention type (ie, treatment versus control) at termination of training expressed in standard deviation units

(M_{post} exp-M_{post} control/SD_{pooled} across groups). This approach assured consistency with previous meta-analyses in this research area.[12,18] Study statistics were converted to *g* using Hedges and Olkin formulas.[25] Pooled standard deviation was calculated using the Rosenthal formula.[24] Effect sizes were characterized as small (0.2), medium (0.5), or large (0.8).[27]

For studies with multiple measures assessing the same domain (eg, working memory), we selected the measure within that domain that was most frequently used across studies to decrease measure heterogeneity. By expressing effect size in standard deviation units, we were able to make a direct comparison of outcomes across studies. Positive effect size values indicated improvement as a result of cognitive interventions for outcomes. When negative effect size values were considered improvements on time-based (ie, decreased task completion time) and self-report outcome measures (ie, decreased symptoms) we multiplied these values by −1 for ease of communication.

Effect-Size Synthesis and Assessment of Heterogeneity. Individual values of *g* were thereafter combined across studies and weighted according to their precision. In this approach, larger sample-size, more precise (less variable) estimates are accorded a greater weight in the creation of the summary effect-size estimate using a random-effects model. Potential differences in effect sizes between studies were analyzed using the method of Hedges and Olkin.[25] This procedure computes mean weighted effect sizes and 95% confidence intervals (CI) for each variable subset and allows for the testing of the influence of each individual factor on the overall results using the Q statistic. To assess stability of underlying effects we used a test for heterogeneity Q_T that is based on the sum of squares of the individual effect sizes around the mean when each square is weighted by the inverse of the estimated variance of the effect size. Q has an asymptotic chi-square distribution and is analogous to the analysis of variance. This approach was complemented by the use of the I^2 statistic that describes the proportion of variability in effect sizes that is attributable to different studies (20% low, 50% moderate, and 75% high heterogeneity).[28] A 2-tailed significance level of $P \leq .05$ was selected for all analyses to provide consistency and comparability of findings with previous meta-analyses in this area.[12,17,18]

Risk of Publication Bias. To partially address the "file-drawer" problem, we calculated a fail-safe N using the Orwin method,[29] which provides an estimate of the number of studies with null results that would be needed to render the obtained effect size not clinically meaningful. In the absence of a universally accepted clinical significance level for effect sizes, we assumed a Hedges' *g* of 0.1 would cease to reflect a meaningful degree of difference between treatment and control groups, as scores from 96% of participants from the 2 groups would overlap at this effect-size.[29]

Moderator Variable Analysis. For analyses of objective cognition, symptoms, or function where there was significant heterogeneity of effect sizes, we evaluated a number of demographic, illness, and treatment moderator variables. Continuous variables evaluated were: sample mean participant age, disease duration, gender distribution, symptoms, estimated IQ, duration of intervention, and study quality. Categorical variables were: early-stage vs chronic sample, in vs outpatient treatment, group vs individual treatment, active vs passive control, use of a computer, drill-and-practice vs drill-and strategy training, therapist-guided treatment, provision of cognitive strategies during therapist coaching, use of a bridging group, CR and control group treated within the context of psychosocial rehabilitation. Continuous data were analyzed with a continuous meta-regression model with a z-test for significance of model fit.[25] Group comparisons were made for categorical moderator variables. In these comparisons, ANOVA-type summary values were estimated for the group effect. All analyses were based on a random-effects model.

Study Quality Measures

We rated each study according to the Clinical Trial Assessment Measure (CTAM).[30] Interrater reliability for this study quality scale was assessed by 2 authors (J.A.L. and M.M.K.) and was 90%. Corresponding authors for each study were also contacted to ensure accuracy of the ratings, of which 55% responded.

Results

Study Characteristics

Sample Characteristics. Seventy-three studies, totaling 4594 participants, satisfied our inclusion and exclusion criteria. Overall, participants were in their mid-to-late 30s (mean age = 37.18 [SD = 7.53]) and mostly men (% male = 66.49 [SD = 13.35]). Additional information on sample characteristics across all studies is provided in table 1.

Treatment Characteristics. In 56 studies, participants interfaced with a computer during CR. In 54 studies, participants were exposed to a therapist during CR; in 25 of those 54, the therapist provided strategy coaching to help facilitate learning. Thirteen studies included a bridging group in addition to CR sessions. CR sessions were administered in a group format in 30 of the studies, and individually in 43 studies. Forty-six studies employed a drill-and-practice approach to CR, while 27 used a drill-and-strategy model. The average length of treatment was 34.86 hours (SD = 23.25), over the course of 13.23 weeks (SD = 7.63), with an average of 2.84 sessions/week (SD = 1.17).

Table 1. Demographic Characteristics of Samples Included in the Meta-Analysis

	Treatment Group				Control Group				Total			
	Mean	SD	Studies	Participants	Mean	SD	Studies	Participants	Mean	SD	Studies	Participants
Age (y)	37.14	7.94	68	2253	37.35	7.90	68	2032	37.18	7.53	73	4594
Gender (% males)	67.25	14.55	64	2120	65.84	14.47	64	1937	66.49	13.35	68	4332
Education (y)	11.69	1.53	56	1892	11.73	1.34	56	1678	11.74	1.36	60	3794
Illness duration (y)	12.46	7.86	45	1473	12.41	7.80	45	1331	12.54	7.56	47	2935
PANSS positive	15.68	4.73	39	1335	15.39	4.83	39	1219	15.77	4.85	41	2731
PANSS negative	18.04	4.46	38	1261	18.30	4.60	38	1143	18.43	4.58	40	2581
IQ	96.47	6.86	34	1106	96.05	8.66	34	1005	96.19	7.30	35	2171
Chlorpromazine equivalents (mg/d)	552.57	288.99	30	1074	568.70	424.21	30	973	563.70	326.21	31	2131
Racial distribution (% non-white)	52.16	25.75	17	525	49.83	24.30	17	438	52.8	27.33	22	1319

Note: PANSS, Positive and Negative Syndrome Scale.

Forty-three studies employed an active control condition; 30 had a passive control. In 33 studies, the CR treatment was embedded in a co-offered psychiatric rehabilitation program, which was provided to both treatment and control groups. For 16 of these 33 studies, rehabilitation programs were evidence-based as defined by the PORT recommendations for psychosocial rehabilitation.[10] The remaining 17 studies did not fit these parameters and were deemed non-evidence-based.

Study Quality. The average score on the CTAM across all 73 studies was 66.04 (SD = 12.81).

Meta-analysis Results

Table 2 includes effect size and heterogeneity calculations for each of the domains tested. Forest plots for significant outcomes are in the supplementary materials.

Effects of Treatment on Cognition. Twenty-six studies provided post-treatment data on global cognition. The overall effect was .29 (95% confidence interval [CI] = .12–.45), indicating a small effect of CR on global cognition. Within the standard cognitive domains of the MCCB, there were significant small-to-moderate effects of CR on verbal learning (k = 61, g = .33), working memory (k = 62, g = .32), attention (k = 35, g = .28), reasoning and problem-solving (k = 50, g = .27), processing speed (k = 52, g = .20), and visual learning (k = 33, g = .19). Effects on social cognition were small and marginally significant (k = 17, g = .12, CI = .00–.24).

Effects of Treatment on Clinical Symptoms. Negative symptoms improved modestly after CR training (k = 31, g = .16). Effects on positive symptoms, total symptoms, and depression were non-significant.

Effects of Treatment on Functioning. There was a small but significant effect of CR on functional outcome as measured by clinician-based assessments and self-reports of community and or work function (k = 34, g = .21). Effects of CR on functional capacity and measures of recovery were non-significant.

Moderator Analysis. Effects of CR on global cognition were greater in interventions that included a bridging group (Q = 6.13, P = .013; figure 2). This effect was largely reproduced in the verbal learning domain (Q = 5.85, P = .016; figure 2). Participants who received strategy coaching performed better on measures of verbal learning (Q = 4.05, P = .044; figure 3) and visual learning (Q = 4.33, P = .038; figure 3). In the attention domain, studies with a longer duration of CR produced larger effects (slope = .023, SE = .011, z = 2.09, P = .036, k = 35).

Sample age, gender, positive and negative symptoms, total psychiatric symptoms, and medication dose played no role in cognitive outcomes. Participants with less formal education improved more on measures of reasoning and

Table 2. Effect Size and Heterogeneity Calculations for Cognitive, Symptomatic, and Functional Outcomes

Outcome	Studies	Effect Size				Heterogeneity				N_{fs}
		Hedge's *g*	95% CI	*z*-Value	*P*-Value	Q-Value	DoF	*P*-Value	I^2	
Global cognition	26	0.29	0.12–0.45	3.43	.001	63.37	25	.000	60.55	49
Attention	35	0.28	0.15–0.42	4.02	.000	82.72	34	.000	58.90	63
Processing speed	52	0.20	0.12–0.29	4.54	.000	71.72	51	.029	28.89	52
Reasoning	50	0.27	0.17–0.38	5.06	.000	96.31	49	.000	49.12	85
Social cognition	17	0.12	0.00–0.24	2.015	.044	16.19	16	.440	1.18	3
Verbal learning	61	0.33	0.24–0.42	6.877	.000	108.01	60	.000	44.45	140
Visual learning	33	0.19	0.06–0.33	2.788	.005	72.67	32	.000	55.97	30
Working memory	62	0.32	0.24–0.40	7.924	.000	80.39	61	.049	24.12	136
Depression	10	0.14	−0.345–0.62	0.552	.581	59.31	9	.000	84.83	N/A
Negative symptoms	31	0.16	0.04–0.29	2.514	.012	52.52	30	.007	42.88	19
Positive symptoms	30	0.04	−0.05–0.13	0.952	.341	17.87	29	.947	0.000	N/A
Total symptoms	22	0.08	−0.06–0.23	1.123	.261	37.05	21	.017	43.33	N/A
Functional capacity	16	0.12	−0.01–0.25	1.804	.071	17.42	15	.294	13.91	N/A
Functional outcome	34	0.21	0.08–0.34	3.21	.001	69.90	33	.000	52.77	37
Recovery	16	0.15	−0.09–0.40	1.23	.220	61.96	15	.000	75.79	N/A

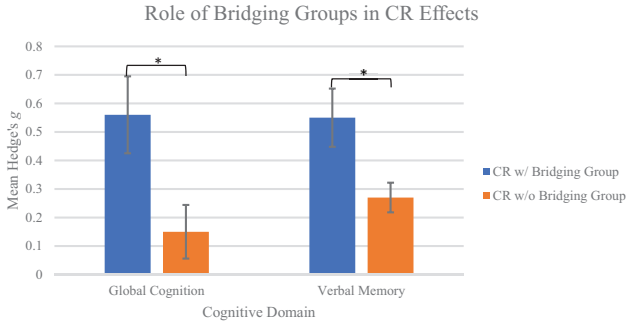

Fig. 2. The effects of bridging groups on global cognition and verbal memory. Error bars show standard error of mean Hedge's *g*. **P* < .05.

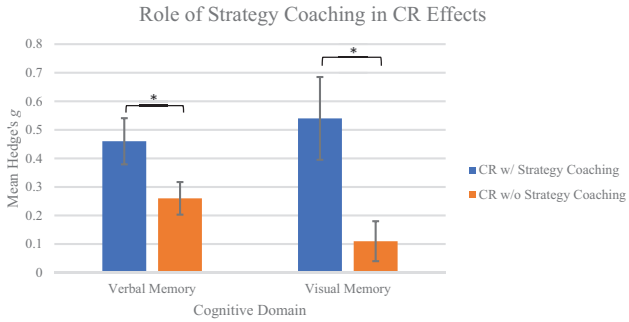

Fig. 3. The effects of strategy coaching on verbal and visual memory. Error bars show standard error of mean Hedge's *g*. **P* < .05.

problem-solving (slope = −.106, SE = .044, *z* = −2.38, *P* = .017, *k* = 43) and processing speed (slope = −.081, SE = .036, *z* = −2.24, *P* = .025, *k* = 43). Samples with lower IQ estimates had larger treatment effects on visual memory (slope = −.023, SE = .010, *z* = −2.36, *P* = .018, *k* = 16). There were larger improvements in function among chronic as compared to early-stage clients (*Q* = 5.87; *g* = .27 chronic, *g* = −.13 early-stage, *P* = .016).

Study quality had an inverse relationship with the size of CR effects on working memory (slope = −.009, SE = .003, *z* = −2.86, *P* = .004, *k* = 62) and reasoning and problem-solving (slope = −.011, SE = .004, *z* = −2.90, *P* = .004, *k* = 50). Improvements in global cognition (*Q* = 4.91, *g* = .57 without active control, *g* = .19 with an active control, *P* = .041), and working memory (*Q* = 5.18, *g* = .43 without active control, *g* = .25 with active control, *P* = .023) were also greater when there was no active control condition.

Discussion

To our knowledge, the current report is the most comprehensive meta-analysis of RCTs of CR for schizophrenia to date. Reporting on findings from 73 unique trials of 4594 participants spanning 18 countries, this study includes data from more than twice as many participants as the last comprehensive meta-analysis in this area,[12] and over 500 more participants than a recently published meta-analysis focused on computerized interventions.[18]

While the present study expands upon previous meta-analyses of CR in size, it also distinguishes itself for its narrowed scope and analytic specificity. Firstly, to isolate the effects of *neurocognitive* training on outcomes, our stringent entry criteria excluded trials of CR with components of social cognitive training that have been included in previous meta-analytic studies in this area.[12,22] Secondly, to our knowledge, this is the first-meta-analysis of CR to analyze the effects of training on subjective recovery-oriented client-experience measures. Thirdly, we assessed the role of multiple treatment-level factors related to CR delivery that cut across diverse curricular models (eg, human guidance, supplementary discussion groups, strategy-coaching, treatment administration format) in an effort to identify the important components of treatment that should be the target of future refinements and adaptations of CR for use in routine clinical practice.

Effects of CR on Treatment Outcomes

Our results illustrate a small-to-moderate effect of CR across multiple cognitive outcomes. We also found small effects of CR on clinician-based assessments and self-reports of community and work function, while CR had no effect on positive or overall psychiatric symptoms, functional capacity, or measures of recovery. While these findings were largely consistent with previous meta-analyses,[12,17,18] we expand preceding reviews by distinguishing between functional outcome and capacity and reporting on the effects of CR on patient-centered measures of recovery and quality of life. Our findings revealed that gains in "real-world" functional outcome in response to CR in the context of a brief clinical trial are possible, and that they are not dependent upon changes in functional capacity, at least as measured in this corpus of studies.

CR in the Context of Psychosocial Rehabilitation

We hypothesized that, consistent with previous findings,[12] effects on functional outcomes would be elevated when CR was delivered along with an adjunctive form of rehabilitation. However, we found no difference in outcomes between trials of stand-alone CR and of CR embedded within other interventions. Neither highly targeted, manualized evidence-based programs nor diversely targeted "treatment mall" style outpatient programs were found to optimize CR outcomes in our analysis. Nonetheless, clear conclusions regarding the role of adjunctive rehabilitation in CR remain elusive for a variety of reasons: First, CR was embedded in a substantial heterogeneity of rehabilitation programs in our dataset with very different targets. This may have increased "noise" and obscured a treatment signal. Second, many authors did not describe details of the CR delivery context or the content of co-occurring treatments, limiting our capacity to analyze these potential moderators. Third, the number of studies that both merged CR with an evidence-based rehabilitation practice (as defined by the 2009 PORT guidelines), as opposed to offering no rehabilitation or not obviously evidence-based practices, and reported functional outcomes, was small ($k = 7$). And fourth, effects of CR-enhanced rehabilitation practices on functional outcomes have been found in some studies to emerge 6 to 12 months after the termination of CR.[31] Current analyses were focused exclusively on outcomes coincident with the termination of CR treatment in each study.

Key Components of CR Delivery: Bridging Groups, Strategy-Coaching, Therapist Presence, and Duration of Treatment

Our findings suggest that a "bridging" group—a discussion group in which clients practice social skills and discuss how cognitive gains can be applied to their everyday lives—may be an integral component of CR delivery, moderating the effect of CR on global cognition and verbal learning. Bridging groups are a key element of several models of CR treatment (eg, Neuropsychological Educational Approach to Cognitive Remediation [NEAR]) and are designed to promote clients' intrinsic motivation and enhance learning outcomes. While findings from neuropsychology have provided a basis for the principles of CR (ie, which cognitive impairments to target), they do not dictate how best to engage clients in learning or promote recovery.[14] Bridging groups are one strategy, giving clients an opportunity to engage with peers to process learning outcomes and discuss applications of cognitive skills in their everyday lives.

The studies captured in our review paint a complex picture, with CR interventions ranging from self-administered drill-and-practice training,[32,33] to therapist-guided paper and pencil practice with manualized strategy provision,[34] to hybrid approaches combining computerized training with coaching and supported employment,[35] to compensatory training approaches, based on teaching the utilization of internal strategies or external prosthetics to overcome cognitive difficulties.[36]

Even when 2 research teams utilized the same computerized training package (eg, COGPACK), delivery varied: in one case, individualized exercises were supplemented with active human instruction and strategy provision,[13] while another described the use of COGPACK with only automated computerized feedback.[37] We found that effects of CR on measures of episodic memory were substantially elevated when delivery included strategy coaching. Given that strategies commonly taught in the context of CR include principles of visualization, chunking, and verbal repetition,[38] it is unsurprising that the greatest effects were evident in episodic memory.

Supplementary Human Guidance (SHG) has previously been defined in the CR literature as encompassing a broad array of therapeutic support that can occur

either during the CR sessions themselves or as part of complementary rehabilitation (eg, employment programs).[18] SHG has been found to enhance some cognitive outcomes in studies of computerized CR.[18] We analyzed this definition with greater precision in several ways. Within studies that provided participants with human guidance during CR sessions, we separated out 2 forms: (1) human presence providing only ad hoc motivation or support, and (2) therapist delivery of explicit strategy-coaching. Furthermore, we chose to analyze adjunctive rehabilitation (which often feature additional therapist interaction) as a separate variable to hone in specifically on the impact of human guidance *during* CR sessions on targeted outcomes. We did not find that motivation or support alone during CR sessions had an effect on CR outcomes. We did find that strategy-coaching improved some cognitive outcomes substantially as compared to CR programs administered without explicit strategy provision. It is possible that the broad definition previously used for SHG conflated the effect of mere human presence during sessions with that of explicit strategy-coaching or supplemental treatment.

Our findings empirically support recommendations from a recent expert working group white paper on CR. This was true despite broader entry criteria in our study with respect to compensatory forms of CR; specifically, experts endorse the importance of clinicians supporting clients in learning strategies and participating in real-world transfer activities.[39] Our results, in conjunction with this set of expert recommendations, suggest that CR sessions should be facilitated by therapists and that these clinicians should receive explicit training on strategy-coaching and bridging group facilitation. With the exception of attention, CR training duration had no effect on cognitive, symptom or functional outcomes.

Participant Characteristics

With the exception of less-educated samples showing an enhanced response to CR in the domains of reasoning and problem-solving and processing speed, and lower baseline estimated IQ predicting larger responses to CR in visual memory, the majority of sample characteristics tested had no impact on outcomes. Thus age, gender, positive, negative and overall psychiatric symptoms, and medication dose should not serve as barriers to benefit from CR interventions. Unexpectedly, more chronically ill samples showed more improvement on functional outcomes in response to CR. These findings may be explained by the fact that these participants had more room for improvement compared to early-stage samples. Additionally, it may reflect that functional assessments in schizophrenia are tuned to deficits common to a more chronic population. Less than 30% of included trials reported on participants' racial demographics, highlighting the need for heightened transparency to critically assess the impact of demographic and sociocultural characteristics on CR outcomes. Given documented disparities in psychosis treatment utilization and long-term outcomes amongst racial-ethnic minority populations,[40–42] future research should collect data on demographic characteristics in order to parse out any predictors of treatment engagement and response. This line of investigation could inform future efforts to engage marginalized populations with traditionally low rates of psychosocial treatment utilization.[43] Such strategies may include enhanced cultural competency in the delivery of CR with diverse populations and the use of recovery-oriented and person-centered approaches, such as addressing unmet social needs (eg, housing) as part of care.[43]

Impact of Study Quality on Treatment Outcomes

Clinical trials that are biased in their sampling, assessment, or related methodology call into question results regarding treatment efficacy. A previous comprehensive meta-analysis of CR found no effect of study quality on outcome.[12] However, in our analysis, studies of higher methodological quality reported lower treatment effects in the domains of working memory and reasoning and problem-solving. In the working memory domain, studies without an active control reported larger effects, suggesting that nonspecific treatment effects may specifically influence measures of working memory.

Study Limitations

The findings of the present study should be interpreted in light of its limitations. First, any meta-analysis using sample means does not provide information on odds of individual participants benefitting from CR. Second, due to multiple comparisons and the use of a threshold *P*-value of .05, some reported findings may have resulted from inflated Type 1 error. However, it should be noted that had we used a more severe alpha of $P = .01$ the majority of findings from this study would remain unchanged. Third, consistent with methods used in previous meta-analyses of CR, we chose only one test within each cognitive domain per study to include in our analysis.[17] Fourth, as is common to most meta-analyses, our findings were dependent upon the fidelity of published reporting of the specific methods of component studies. Given the multifaceted differences in approach to CR evident in the literature, along with the complexity of the intervention itself (curriculum, role, and training of treatment facilitators, treatment setting etc.), failures to detail specific features of treatment administration in specific studies may have introduced unintended noise into our analyses.

Future Directions

The 2020 American Psychiatric Association practice guidelines for the treatment of schizophrenia described CR as a "suggested," rather than "recommended" practice, citing low research evidence of CR's impact on global, social, and occupational functioning and core illness symptoms.[11] The current comprehensive meta-analysis of a substantial research base reveals that in fact CR produces robust, small-to-moderate effects on a broad-range of core treatment targets (cognition) and robust albeit small effects on the more clinically relevant domain of psychosocial function. Future research should aim to further parse out the active ingredients of CR and the optimal settings for delivery. Our findings elucidate the potential benefit of therapist strategy-coaching and bridging groups to enhance cognitive outcomes. However, while the ultimate goal of both strategy-coaching and bridging groups is to promote cognitive strategy use in daily life outside of treatment, more research is needed to pinpoint the factors that ensure transference of these cognitive gains to functional outcomes. Future investigation is also needed to understand the utility of CR as an adjunctive feature to another psychosocial intervention. Indeed, the number of studies merging CR with evidence-based psychosocial rehabilitation programs remains low, inhibiting assessment of the role CR may play in enhancing outcomes of other treatments. Lastly, 33% (k = 18) of the therapist-delivered CR trials captured in our review did not report on the level of training of the CR interventionists, which may influence the replicability of treatment findings and have an impact on fidelity of CR interventions to treatment protocols when administered in real-world clinical settings. In accordance with recent recommendations from the CR expert working group, future reports of CR should specify therapists' level of background.[39]

Conclusions

A meta-analysis of 73 unique RCTs (4594 participants) of CR revealed small-to-moderate effects on all cognitive domains studied (primary outcome). Small effects were evident on client and clinician-reported psychosocial function (secondary outcomes). No effects were evident on symptoms, capacity-measures of function, or measures of recovery. CR interventions with a bridging group and strategy-coaching were more cognitively potent. Future research should investigate approaches to modifying CR to increase its impact on functional outcomes.

This comprehensive review of CR also highlights the need for increased collection and reporting of demographic and sociocultural factors and client-centered measures of quality of life and recovery to ensure that CR interventions are meeting the needs of diverse client populations.

Supplementary Material

Supplementary material is available at *Schizophrenia Bulletin* online.

Acknowledgment

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References

1. Fett A-KJ, Velthorst E, Reichenberg A, et al. Long-term changes in cognitive functioning in individuals with psychotic disorders: findings from the Suffolk County Mental Health Project. *JAMA Psychiatry*. 2020;77(4):387. doi:10.1001/jamapsychiatry.2019.3993
2. Schaefer J, Giangrande E, Weinberger DR, Dickinson D. The global cognitive impairment in schizophrenia: consistent over decades and around the world. *Schizophr Res*. 2013;150(1):42–50. doi:10.1016/j.schres.2013.07.009
3. Green MF, Llerena K, Kern RS. The "Right Stuff" revisited: what have we learned about the determinants of daily functioning in schizophrenia? *Schizophr Bull*. 2015;41(4):781–785. doi:10.1093/schbul/sbv018
4. Green MF, Kern RS, Heaton RK. Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophr Res*. 2004;72(1):41–51. doi:10.1016/j.schres.2004.09.009
5. Fett A-KJ, Viechtbauer W, Dominguez M-G, Penn DL, van Os J, Krabbendam L. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. *Neurosci Biobehav Rev*. 2011;35(3):573–588. doi:10.1016/j.neubiorev.2010.07.001
6. Halverson TF, Orleans-Pobee M, Merritt C, Sheeran P, Fett A-K, Penn DL. Pathways to functional outcomes in schizophrenia spectrum disorders: meta-analysis of social cognitive and neurocognitive predictors. *Neurosci Biobehav Rev*. 2019;105:212–219. doi:10.1016/j.neubiorev.2019.07.020
7. Fiszdon JM, Choi J, Goulet J, Bell MD. Temporal relationship between change in cognition and change in functioning in schizophrenia. *Schizophr Res*. 2008;105(1–3):105–113. doi:10.1016/j.schres.2008.06.010
8. Wykes T, Reeder C, Huddy V, et al. Developing models of how cognitive improvements change functioning: mediation, moderation and moderated mediation. *Schizophr Res*. 2012;138(1):88–93. doi:10.1016/j.schres.2012.03.020
9. Keefe RSE, Vinogradov S, Medalia A, et al. Report from the working group conference on multisite trial design for cognitive remediation in schizophrenia. *Schizophr Bull*. 2011;37(5):1057–1065. doi:10.1093/schbul/sbq010
10. Dixon LB, Dickerson F, Bellack AS, et al. The 2009 schizophrenia PORT psychosocial treatment recommendations and summary statements. *Schizophr Bull*. 2010;36(1):48–70. doi:10.1093/schbul/sbp115
11. Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry*. 2020;177(9):868–872. doi:10.1176/appi.ajp.2020.177901
12. Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatry*. 2011;168(5):472–485. doi:10.1176/appi.ajp.2010.10060855

13. Bryce SD, Rossell SL, Lee SJ, et al. Neurocognitive and self-efficacy benefits of cognitive remediation in schizophrenia: a randomized controlled trial - corrigendum. *J Int Neuropsychol Soc JINS*. 2019;25(6):659–660. doi:10.1017/S1355617719000535
14. Medalia A, Freilich B. The neuropsychological educational approach to cognitive remediation (NEAR) model: practice principles and outcome studies. *Am J Psychiatr Rehabil*. 2008;11(2):123–143. doi:10.1080/15487760801963660
15. Gharaeipour M, Scott B. Effects of cognitive remediation on neurocognitive functions and psychiatric symptoms in schizophrenia inpatients. *Schizophr Res*. 2012;142(1):165–170. doi:10.1016/j.schres.2012.09.018
16. Au DWH, Tsang HWH, So WWY, et al. Effects of integrated supported employment plus cognitive remediation training for people with schizophrenia and schizoaffective disorders. *Schizophr Res*. 2015;166(1):297–303. doi:10.1016/j.schres.2015.05.013
17. Prikken M, Konings MJ, Lei WU, Begemann MJH, Sommer IEC. The efficacy of computerized cognitive drill and practice training for patients with a schizophrenia-spectrum disorder: a meta-analysis. *Schizophr Res*. 2019;204:368–374. doi:10.1016/j.schres.2018.07.034
18. Kambeitz-Ilankovic L, Betz LT, Dominke C, et al. Multi-outcome meta-analysis (MOMA) of cognitive remediation in schizophrenia: revisiting the relevance of human coaching and elucidating interplay between multiple outcomes. *Neurosci Biobehav Rev*. 2019;107:828–845. doi:10.1016/j.neubiorev.2019.09.031
19. Moher D. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151(4):264. doi:10.7326/0003-4819-151-4-200908180-00135
20. The Diagnostic and Statistical Manual of Mental Disorders-III (DSM-III). New York: American Psychiatric Association; 1980.
21. Nuechterlein KH, Green MF, Kern RS, et al. The MATRICS consensus cognitive battery, Part 1: test selection, reliability, and validity. *Am J Psychiatry*. 2008;165(2):203–213. doi:10.1176/appi.ajp.2007.07010042
22. McGurk SR, Twamley EW, Sitzer DI, McHugo GJ, Mueser KT. A meta-analysis of cognitive remediation in schizophrenia. *Am J Psychiatry*. 2007;164(12):1791–1802. doi:10.1176/appi.ajp.2007.07060906
23. Harvey PD, Velligan DI, Bellack AS. Performance-based measures of functional skills: usefulness in clinical treatment studies. *Schizophr Bull*. 2007;33(5):1138–1148. doi:10.1093/schbul/sbm040
24. Rosenthal R. *Meta-Analytic Procedures for Social Research*. Thousand Oaks, CA: SAGE Publications, Inc.; 1991. doi:10.4135/9781412984997
25. Hedges LV, Olkin I. *Statistical Methods for Meta-Analysis*. Orlando, FL: Academic Press; 1985.
26. Borenstein M, Hedges L, Higgins J, Rothstein H. Comprehensive Meta-Analysis Version 2. Englewood, NJ: Biostat; 2005:104.
27. Cohen J 2nd. *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
28. Higgins JPT. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–560. doi:10.1136/bmj.327.7414.557
29. Orwin RG. A Fail-SafeN for effect size in meta-analysis. *J Educ Stat*. 1983;8:157–159. doi:10.3102/10769986008002157
30. Tarrier N, Wykes T. Is there evidence that cognitive behaviour therapy is an effective treatment for schizophrenia? A cautious or cautionary tale? *Behav Res Ther*. 2004;42(12):1377–1401. doi:10.1016/j.brat.2004.06.020
31. Bell MD, Bryson GJ, Greig TC, Fiszdon JM, Wexler BE. Neurocognitive enhancement therapy with work therapy: productivity outcomes at 6- and 12-month follow-ups. *J Rehabil Res Dev*. 2005;42(6):829. doi:10.1682/JRRD.2005.03.0061
32. Fisher M, Loewy R, Carter C, et al. Neuroplasticity-based auditory training via laptop computer improves cognition in young individuals with recent onset schizophrenia. *Schizophr Bull*. 2015;41(1):250–258. doi:10.1093/schbul/sbt232
33. Moritz S, Thoering T, Kühn S, Willenborg B, Westermann S, Nagel M. Metacognition-augmented cognitive remediation training reduces jumping to conclusions and overconfidence but not neurocognitive deficits in psychosis. *Front Psychol*. 2015;6. doi:10.3389/fpsyg.2015.01048
34. Wykes T, Reeder C. *Cognitive Remediation Therapy for Schizophrenia: Theory and Practice*. London; New York: Routledge; 2005.
35. McGurk SR, Mueser KT, Pascaris A. Cognitive training and supported employment for persons with severe mental illness: one-year results from a randomized controlled trial. *Schizophr Bull*. 2005;31(4):898–909. doi:10.1093/schbul/sbi037
36. Twamley EW, Savla GN, Zurhellen CH, Heaton RK, Jeste DV. Development and pilot testing of a novel compensatory cognitive training intervention for people with psychosis. *Am J Psychiatr Rehabil*. 2008;11(2):144–163. doi:10.1080/15487760801963678
37. Moritz S, Veckenstedt R, Bohn F, et al. Complementary group Metacognitive Training (MCT) reduces delusional ideation in schizophrenia. *Schizophr Res*. 2013;151(1–3):61–69. doi:10.1016/j.schres.2013.10.007
38. Barlati S, Deste G, De Peri L, Ariu C, Vita A. Cognitive remediation in schizophrenia: current status and future perspectives. *Schizophrenia Research and Treatment*. doi:10.1155/2013/156084
39. Bowie CR, Bell MD, Fiszdon JM, et al. Cognitive remediation for schizophrenia: an expert working group white paper on core techniques. *Schizophr Res*. 2020;215:49–53. doi:10.1016/j.schres.2019.10.047
40. Eack SM, Newhill CE. Racial disparities in mental health outcomes after psychiatric hospital discharge among individuals with severe mental illness. *Soc Work Res*. 2012;36(1):41–52. doi:10.1093/swr/svs014
41. Morgan C, Fearon P, Lappin J, et al. Ethnicity and long-term course and outcome of psychotic disorders in a UK sample: the ÆSOP-10 study. *Br J Psychiatry*. 2017;211(2):88–94. doi:10.1192/bjp.bp.116.193342
42. Oluwoye O, Stiles B, Monroe-DeVita M, et al. Racial-ethnic disparities in first-episode psychosis treatment outcomes from the RAISE-ETP study. *Psychiatr Serv*. 2018;69(11):1138–1145. doi:10.1176/appi.ps.201800067
43. Dixon LB, Holoshitz Y, Nossel I. Treatment engagement of individuals experiencing mental illness: review and update. *World Psychiatry*. 2016;15(1):13–20. doi:10.1002/wps.20306